



FH gene

fumarate hydratase

Normal Function

The *FH* gene provides instructions for making an enzyme called fumarase (also known as fumarate hydratase). Fumarase participates in an important series of reactions known as the citric acid cycle or Krebs cycle, which allows cells to use oxygen and generate energy. Specifically, fumarase helps convert a molecule called fumarate to a molecule called malate.

Health Conditions Related to Genetic Changes

fumarase deficiency

Approximately 17 *FH* gene mutations that cause fumarase deficiency have been reported. Fumarase deficiency occurs in individuals who inherit two mutated copies of the *FH* gene in each cell. Most of these mutations replace one protein building block (amino acid) with another amino acid in the fumarase enzyme. These changes disrupt the ability of the enzyme to help convert fumarate to malate, interfering with the function of this reaction in the citric acid cycle. Impairment of the process that generates energy for cells is particularly harmful to cells in the developing brain, and this impairment results in the signs and symptoms of fumarase deficiency.

hereditary leiomyomatosis and renal cell cancer

Approximately 50 mutations in the *FH* gene that cause hereditary leiomyomatosis and renal cell cancer (HLRCC) have been reported. Most of these mutations replace one amino acid with another amino acid in the fumarase enzyme.

People with HLRCC are born with one mutated copy of the *FH* gene in each cell. The second copy of the *FH* gene in certain cells may also acquire mutations as a result of environmental factors such as ultraviolet radiation from the sun or a mistake that occurs as DNA copies itself during cell division. These changes are called somatic mutations and are not inherited.

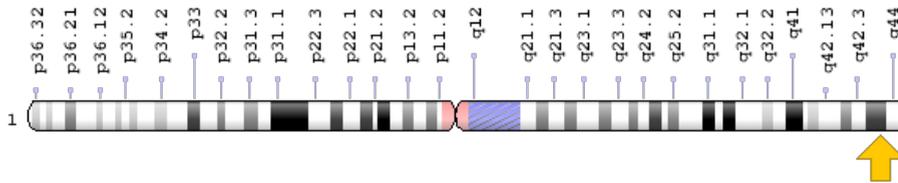
FH gene mutations may interfere with the enzyme's role in the citric acid cycle, resulting in a buildup of fumarate. Researchers believe that the excess fumarate may interfere with the regulation of oxygen levels in the cell. Chronic oxygen deficiency (hypoxia) in cells with two mutated copies of the *FH* gene may encourage tumor formation and result in the tendency to develop leiomyomas and renal cell cancer.

primary macronodular adrenal hyperplasia

Chromosomal Location

Cytogenetic Location: 1q43, which is the long (q) arm of chromosome 1 at position 43

Molecular Location: base pairs 241,497,557 to 241,519,785 on chromosome 1 (Homo sapiens Annotation Release 108, GRCh38.p7) (NCBI)



Credit: Genome Decoration Page/NCBI

Other Names for This Gene

- fumarase
- fumarase hydratase
- FUMH_HUMAN
- HLRCC
- LRCC
- MCL
- MCUL1

Additional Information & Resources

Educational Resources

- Biochemistry (fifth edition, 2002): The Citric Acid Cycle Oxidizes Two-Carbon Units
<https://www.ncbi.nlm.nih.gov/books/NBK22427/>

GeneReviews

- Fumarate Hydratase Deficiency
<https://www.ncbi.nlm.nih.gov/books/NBK1506>
- Hereditary Leiomyomatosis and Renal Cell Cancer
<https://www.ncbi.nlm.nih.gov/books/NBK1252>

Scientific Articles on PubMed

- PubMed
<https://www.ncbi.nlm.nih.gov/pubmed?term=%28%28FH%5BTIAB%5D%29+OR+%28fumarate+hydratase%5BTIAB%5D%29%29+AND+%28%28fumarase%5BMAJR%5D%29+OR+%28fumarate+hydratase%5BMAJR%5D%29%29+AND+%28%28Genes%5BMH%5D%29+OR+%28Genetic+Phenomena%5BMH%5D%29%29+AND+english%5Bla%5D+AND+human%5Bmh%5D+AND+%22last+1800+days%22%5Bdp%5D>

OMIM

- FUMARATE HYDRATASE
<http://omim.org/entry/136850>

Research Resources

- Atlas of Genetics and Cytogenetics in Oncology and Haematology
<http://atlasgeneticsoncology.org/Genes/FHID40573ch1q42.html>
- ClinVar
<https://www.ncbi.nlm.nih.gov/clinvar?term=FH%5Bgene%5D>
- HGNC Gene Symbol Report
http://www.genenames.org/cgi-bin/gene_symbol_report?q=data/hgnc_data.php&hgnc_id=3700
- NCBI Gene
<https://www.ncbi.nlm.nih.gov/gene/2271>
- UniProt
<http://www.uniprot.org/uniprot/P07954>

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